

Using human embryonic stem cells to treat radiation-induced stem cell loss: Benefits vs cancer risk

Grant Award Details

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Grant Type: SEED Grant

Grant Number: RS1-00413

Project Objective: this is the NCE report which the PI had requested to further detail their transplant work in irradiated animals, as well as the work on characterizing the radioresponse of human neural stem cells.
Ongoing CNS studies:
PI reports some unpublished data, emphasizing follow-up work with human neural stem cells that show the capability of these multipotent stem cells to restore cognitive function in irradiated rats.

Investigator:

Name: Charles Limoli
Institution: University of California, Irvine
Type: PI

Disease Focus: Cancer, Neurological Disorders, Skeletal/Smooth Muscle disorders

Human Stem Cell Use: Embryonic Stem Cell

Award Value: \$593,242

Status: Closed

Progress Reports

Reporting Period: Year 2

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Reporting Period: NCE

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Grant Application Details

Application Title: Using human embryonic stem cells to treat radiation-induced stem cell loss: Benefits vs cancer risk

Public Abstract: A variety of stem cells exist in humans throughout life and maintain their ability to divide and change into multiple cell types. Different types of adult derived stem cells occur throughout the body, and reside within specific tissues that serve as a reserve pool of cells that can replenish other cells lost due to aging, disease, trauma, chemotherapy or exposure to ionizing radiation. When conditions occur that lead to the depletion of these adult derived stem cells the recovery of normal tissue is impaired and a variety of complications result. For example, we have demonstrated that when neural stem cells are depleted after whole brain irradiation a subsequent deficit in cognition occurs, and that when muscle stem cells are depleted after leg irradiation an accelerated loss of muscle mass occurs. While an increase in stem cell numbers after depletion has been shown to lead to some functional recovery in the irradiated tissue, such recovery is usually very prolonged and generally suboptimal. Ionizing radiation is a physical agent that is effective at reducing the number of adult stem cells in nearly all tissues. Normally people are not exposed to doses of radiation that are cause for concern, however, many people are subjected to significant radiation exposures during the course of clinical radiotherapy. While radiotherapy is a front line treatment for many types of cancer, there are often unavoidable side effects associated with the irradiation of normal tissue that can be linked to the depletion of critical stem cell pools. In addition, many of these side effects pose particular threats to pediatric patients undergoing radiotherapy, since children contain more stem cells and suffer higher absolute losses of these cells after irradiation. Based on the foregoing, we will explore the potential utility and risks associated with using human embryonic stem cells (hESC) in the treatment of certain adverse effects associated with radiation-induced stem cell depletion. Our experiments will directly address whether hESCs can be used to replenish specific populations of stem cells in the brain and muscle depleted after irradiation in efforts to prevent subsequent declines in cognition and muscle mass respectively. In addition to using hESC to hasten the functional recovery of tissue after irradiation, we will also test whether implantation of such unique cells holds unforeseen risks for the development of cancer. Evidence suggests that certain types of stem cells may be prone to cancer, and since little is known regarding this issue with respect to hESC, we feel this critical issue must be addressed. Thus, we will investigate whether hESC implanted into animals develop into tumors over time. The studies proposed here comprise a first step in determining how useful hESCs will be in the treatment of humans exposed to ionizing radiation, as well as many other diseases where adult stem cell depletion might be a concern.

Statement of Benefit to California: Radiotherapy is a front line treatment used in California for many types of cancer, including brain, breast, prostate, bone and other cancer types presenting surgical complications. Treatment of these cancers through the use of radiation is however, often associated with side effects caused by the depletion of critical stem cell pools contained within non-cancerous normal tissue. While radiotherapy is clearly beneficial overall, many of these side effects have no viable treatment options. If we can demonstrate that human embryonic stem cells (hESC) hold promise as a safe therapeutic agent for the treatment of radiation-induced stem cell depletion, then cancer patients may have a new treatment for countering many of the debilitating side effects associated with radiotherapy. Once developed this new technology could position California to attract cancer patients throughout the United States, and the state would clearly benefit from the increased economic activity associated with a rise in patient numbers.

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